Early Collaboration Meetings Under the FDA Modernization Act (FDAMA), Guidance for Industry and CDRH Staff

This document is intended to provide guidance. It represents the Agency's current thinking on the above. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

Office of the Center Director

Document issued on: February 19, 1998

Until May 26, 1998, comments and suggestions regarding this document should be submitted to Docket No. 98D-0078, Dockets Management Branch, Division of Management Systems and Policy, Office of Human Resources and Management Services, Food and Drug Administration, 12420 Parklawn Drive (HFA-305), Room 1-23, Rockville, MD 20857. Such comments will be considered when determining whether to amend the current guidance.

After May 26, 1998, comments and suggestions may be submitted at any time for Agency consideration to, Kathy M. Poneleit, 9200 Corporate Blvd, HFZ-402, Rockville, MD 20850. Comments may not be acted upon by the Agency until the document is next revised or updated. For questions regarding the use or interpretation of this guidance contact Kathy M. Poneleit or Lisa C. Fisher at 301-594-2186.

Additional Copies: World Wide Web/CDRH home page at http://www.fda.gov/cdrh or CDRH Facts on Demand at 1-800-899-0381 or 301-827-0111, specify number 310 when prompted for the document shelf number.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration
Center for Devices and Radiological Health
Rockville, MD 20850

GUIDANCE ON STANDARD OPERATING PROCEDURES

Early Collaboration Meetings Under the FDA Modernization Act of 1997 (FDAMA), Guidance[1] for Industry and CDRH Staff

The FDAMA provides for two early collaboration meetings. These meetings are intended to facilitate interaction between FDA and applicants and provide clear direction for testing and development of those products requiring clinical investigations to support marketing.

Determination Meeting

One meeting, described in new §513(a)(3)(D), is available to anyone anticipating submitting a PMA and is intended to provide the applicant with the agency's determination of the type of valid scientific evidence that will be necessary to demonstrate that the device is effective for its intended use. This pre-PMA meeting is to focus on the broad outline of the clinical trial design. As a result of this meeting, FDA generally will determine whether clinical studies with concurrent randomized controls, concurrent non-randomized controls, historical controls, or other types of evidence will be acceptable to the agency. FDA's determination is to be written, shared with the applicant within 30 days following the meeting, and is binding, unless it would be contrary to public health.

Agreement Meeting

The other opportunity for a meeting established by the FDAMA is a pre-IDE meeting, described in new §520(g)(7), which is open to any person planning to investigate the safety or effectiveness of a class III product or any implant. The purpose of this meeting is to reach agreement on the investigational plan, including the clinical protocol. The investigational plan includes the statement of the purpose of the investigation, protocol, risk analysis, description of the device, monitoring procedures, labeling, informed consent materials, IRB information, and list of study institutions (see 21 CFR 812.25). Any agreement reached in this meeting is also to be written, shared with the sponsor, and made part of the administrative record. It, too, is binding on the agency and the sponsor. It can be changed only with the written agreement of the sponsor or when there is a substantial scientific issue essential to determining the safety or effectiveness of the device.

Background

[1] **This document is intended to provide guidance. It represents the Agency's current thinking on the above. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.**

The agency believes that one meeting will often be able to accomplish the objectives of both provisions of FDAMA. However, FDA understands that some sponsors will request and benefit from two separate meetings.

The meeting(s) should take place early in the development of the product so the sponsor may use the agency's determination/agreement to plan efficiently for the clinical investigation. However, FDAMA also recognizes that the agency will not be able to reach useful conclusions unless a fair amount of planning and commitment has been undertaken by the sponsor prior to the meeting. Therefore, both provisions provide that the sponsor requesting a meeting shall include (1) a detailed description of the device; (2) a detailed description of the proposed conditions of use; (3) a proposed plan for determining whether there is a reasonable assurance of effectiveness; (4) if available, information regarding the expected performance of the device; and (5) (for the pre-IDE agreement meeting) a detailed clinical protocol.

The FDAMA makes it clear that the determinations or agreements resulting from these meetings are to be binding. In the case of a meeting under §513(a)(3), the agency's determination with respect to valid scientific evidence cannot be changed unless FDA concludes that adhering to it could be contrary to public health. Further, in deciding what type of studies should be conducted, the agency is charged with considering, in consultation with the applicant, the least burdensome way of evaluating device effectiveness that has a reasonable likelihood of success, and determining that any clinical data specified are necessary to evaluate effectiveness. In the case of an agreement reached under §520(g)(7), the agency is authorized to change the agreement only when a substantial scientific issue essential to determining the safety or effectiveness of the device has been identified, and only following an opportunity for the sponsor to meet with FDA to discuss the scientific issue involved.

The binding nature of the agreement or determination is predicated on the manufacturer not significantly changing the parameters underlying the agreement or determination (e.g., intended use and indications, product design, investigational plan, clinical study protocol, etc.). If these parameters are changed, then the basis for the agreement or determination will have been abrogated and the agency's agreement or determination will be no more influential on its decision making than any other general agency advice.

The FDAMA provisions do not address the status of other pre-submission meetings or address consideration of other topics. If applicants choose not to request meetings pursuant to these two new provisions, then CDRH should continue to meet with them for standard pre-IDE meetings, as has been done for several years. Similarly, during a §513(a)/520(g) meeting, other topics, such as the value of feasibility studies, pre-clinical animal evaluation, clinical studies of safety, etc., are likely to arise; they should be addressed, but are not

appropriately included in the binding agreement/agency determination. The meetings envisioned in the law also are not pre-PMA submission meetings to discuss formatting of the application or the suitability of a clinical data set already produced by a potential PMA applicant. These pre-PMA submission meetings should also continue to be held. However, in such cases, CDRH staff should clarify to applicants that the meeting is intended to help them develop plans or finish a PMA submission, but is not an FDAMA mandated meeting that will result in a binding agency commitment.

Expectations of the Applicant/Sponsor

The FDAMA requires and the Agency expects the meeting request to be accompanied by certain information. To make such a meeting useful, a meeting request by the applicant should include, where applicable, the following information:

1. A detailed description of the device;

    - its composition/components,
    - engineering drawings,
    - mechanism of action/principles of operation, and
    - analysis of potential failure modes.

2. A detailed description of the proposed conditions of use:

    - a statement of the proposed intended use and indications,
    - population for whom use is indicated,
    - a summary of instructions for use of the product,
    - relevant warnings, precautions and contraindications, and
    - any proposed restrictions or training requirements.

3. A proposed plan for determining whether there is a reasonable assurance of effectiveness:

    - risk analysis,
    - primary and secondary endpoints/objectives and how they will be measured,
    - comparison group/comparison product against which the effect will be measured,
    - how the results in that comparison group/comparison product is or will be documented,
    - projected effect size of the product on the endpoint,
    - number of study sites,
    - projected sample size, and

- statistical analysis model.

4. Available performance information:

    - in vitro test data with the test protocol, objectives and endpoints,
    - a summary of animal test data, and
    - a summary of clinical (or clinical laboratory) experience.

5. For a meeting requested pursuant to 520(g)(7), proposed protocol for a clinical trial:

    - inclusion and exclusion criteria,
    - items to be monitored,
    - monitoring schedule,
    - planned statistical analysis,
    - Data Safety Monitoring Board operations,
    - Informed Consent materials,
    - IRB information, and
    - list of study information.

The agency expects that this information ordinarily may be presented to the agency in a document of approximately 10 - 20 pages in length, with only those appendices necessary for clarity of the presentation. In addition to providing the detailed information regarding the product, FDA expects the applicant/sponsor to indicate a preference for when and how they wish to meet (e.g. teleconference, video conference, face to face), provide a draft agenda, and indicate the length of time they anticipate they would like for discussion.

Expectations of the Agency

- Within 30 days of receiving a request accompanied by the required information, the relevant division will promptly schedule meetings requested by companies.

- FDA attendees will be determined by the division. The meetings ordinarily will include three to six FDA Staff: a project manager or lead scientist with responsibility for the product area, medical officer, statistician, other key product scientists (e.g. materials expert) from ODE, OC, OSB and/or OST, the review branch chief, and a division associate director, deputy director, or division director.

- For meetings likely to consider novel products, development strategies, claim structures, or controversial issues, the division will discuss the issue with

and, if appropriate, schedule the meeting to include participation by the Director or Deputy Director of the Office of Device Evaluation.

- Program Operations Staff (POS) will be notified of planned meetings to track and maintain the administrative record and the follow-up correspondence to the applicant.

- Agency staff to attend the meeting will ordinarily conduct a pre-meeting at which they will discuss questions raised by the request of the applicant, review experience with similar applications or similar products, and formulate a tentative proposal for responding to the applicant's proposal.

- Meetings with the applicant may be face to face, by video conference, or teleconference. Meetings will be scheduled with sufficient time to adequately explore and work through the issues --- typically for up to two hours.

- The agency's lead review scientist or branch chief will routinely be responsible for introducing Agency staff at the meetings, describing the Agency's understanding of the applicant's proposal (based upon the information submitted), and opening the discussion.

- The company will be given an opportunity to present information that it believes is relevant to the discussion as well as to answer agency inquiries. Ordinarily, at the end of the meeting, the senior FDA member present with responsibility for the application will recapitulate any agreements reached and identify issues which have been discussed but on which agreement has not been reached.

- A record of attendees and minutes of the meeting will be made by a previously designated Agency attendee. The minutes are to be in sufficient detail to reflect the substance of scientific issues discussed at the meeting as well as any agreements or resolution of those issues reached by the participants.

- The FDA staff member with the responsibility for recording the minutes of the meeting shall also separately prepare (or use the minutes of the meeting as) a memorandum of agreement [§520(g)] or memorandum of agency determinations [§513(a) meeting]. This memorandum will record the Agency's determination with respect to valid scientific evidence and/or commitments on the study design. Within two weeks of the meeting, a draft of this memorandum will be circulated for review among the FDA participants. It will then be signed by the Division Director (upon concurrence of Director/Deputy Director of ODE with the draft), conveyed to the applicant within 30 days of the meeting, and placed in the administrative file.